REMARKS/ARGUMENT

Claims 1, 3-4, 8-27, 29, 31, 32, 35-44, 51, 53, 55-75, 78, 79, 83, 84, 86, 88-89, and 91-100 were pending following Applicants' Amendment and Response filed on March 26, 2008. Applicants respectfully indicate that the listing of pending claims in the Office Action Summary, item 4, and in paragraph 1 of the June 26, 2008 Office Action ("Office Action") does not reflect all of the then-pending claims. Of the then-pending claims which were not listed in paragraph 1, claims 8, 31, 32, 56, 57, 58, 66, 79, 84, 88, 89, and 91 were examined in the Office Action (*see* Office Action at paragraphs 10-14), while claims 78 and 100 were not addressed.

In this paper, claims 1, 3, 4, 10-14, 16-17, 20, 23-27, 37-39, 41-44, 51, 53, 57-58, 60-62, 64, 66-72, 75, 78-79, 93, 95-96, and 98-100 are amended, and claims 15, 36, 40, 59, 83, 94 and 97 are canceled without prejudice or disclaimer. Applicants reserve the right to pursue the canceled subject matter in future applications. With the entry of this amendment, claims 1, 3-4, 8-14, 16-27, 29, 31-32, 35, 37-39, 41-44, 51, 53, 55-58, 60-75, 78-79, 84, 86, 88-89, 91-93, 95-96, and 98-100 are pending in this application.

Claim 1 is amended to recite affinity molecule/charged carrier molecule conjugates as the substance with which the sample is contacted. Support for this amendment is found at least in original claim 10 and paragraphs [0017], [0021], and [0079] of the specification. Claims 1, 39, 42, 51, and 93 are amended to recite that the charged carrier molecule has a net negative charge. Support for this amendment is found at least in original claim 15, paragraph [0084], and paragraph [0053], lines 3-6 of the specification. Claims 1, 39, 42, 51, and 93 are amended to recite that the charged carrier molecule causes a change in a separation or migration property of the analyte by binding of the conjugate to the analyte. Support for this amendment is found at

least in original claim 10 and paragraphs [0081]-[0083] of the specification. Claims 1, 39, 42, 51, and 93 are amended to recite that the polyanion binds interfering sample constituents that would otherwise bind non-specifically to the charged carrier molecule. Support for this amendment is found at least at paragraphs [0052] and [0192] of the specification.

Support for the amendment to claim 10 reciting further contacting the analyte with a non-conjugated affinity molecule is found at least in original claims 1 and 10 and paragraph [0022] of the specification. Support for the amendment to claim 38 is also found at least in paragraph [0022] of the specification. Support for the amendment to claim 39 is found at least in paragraphs [0024] and [0151] of the specification. Support for the amendment to claim 41 is found at least in paragraphs [0025] and [0152] of the specification. Support for the amendment to claim 42 is found at least in paragraphs [0026] and [0153] of the specification. The amendments to claims 3, 4, 11-14, 16-17, 20, 23-27, 37, 43-44, 53, 57-58, 60-62, 64, 66-72, 75, 78-79, 95-96, and 98-100 are presented for clarity and consistency, or to update claim dependencies.

All of the above amendments either are supported by the specification and/or the original claims or are of a minor clerical nature. Accordingly, the amendments add no new matter. Applicants respectfully request reconsideration of the pending claims in the application.

I. Claim Rejections Under 35 U.S.C. § 102 - Anticipation

Claims 1, 3-4, 9-27, 29, 35-44, 51, 53, 55, 59-65, 67-75, 83, 86, and 92-99 were rejected under 35 U.S.C. § 102(b) for allegedly being anticipated by European patent application publication EP 1376126 A1 to Kawabata et al. ("Kawabata"). Applicants respectfully traverse these rejections for the reasons set forth below.

First, Applicants note that the European application of Kawabata was not published until January 2, 2004, which is less than one year before the non-provisional filing date of the subject application (April 8, 2004). Accordingly, Applicants respectfully request that the Office not apply the European publication of the Kawabata reference to a rejection under § 102(b). Moreover, Kawabata was published after the filing date (September 4, 2003) of at least the second provisional application to which priority is claimed. In view of the disclosure therein, and the priority date which precedes the Kawabata EP publication, Applicants respectfully request that the Office remove the European publication of Kawabata as a prior art reference and not base any rejections on this reference.

To anticipate a claim, a reference must teach every element of the claim. *See* MPEP § 2131. Even if a reference teaches every element of a claim, it does not anticipate unless it discloses "the elements of the claimed invention arranged as in the claim." *Id.*; *see also Net MoneyIn, Inc. v. VeriSign, Inc.*, No. 2007-1565, 2008 App. LEXIS 21827 at *24 (Fed. Cir. October 20, 2008). In view of the amendments to the pending claims, particularly the amendments to independent claims 1, 39, 42, 51, and 93, Kawabata does not disclose every element of the these claims, and therefore cannot anticipate the claimed invention. If an independent claim is not anticipated, none of its dependent claims can be anticipated either. Accordingly, the dependent claims, which all depend from either claim 1, 39, 42, 51, or 93, also cannot be anticipated by Kawabata.

Applicants have amended independent claims 1, 39, 51, and 93 to include a charged carrier molecule which has a net negative charge. In these claims, the charged carrier molecule is conjugated with an affinity molecule. As a result, the claims require, among other limitations:

- contacting the sample with an affinity molecule/charged carrier molecule conjugate, and
- electrophoretically separating (claims 1, 39, and 93) or concentrating (claim 51) the materials using a separation/concentration channel filled with a separation/concentration media, and
- wherein the separation/concentration channel also includes a polyanion.

Kawabata does not teach any of these limitations.

As set forth in the Office Action, Kawabata teaches contacting a target with nucleic acid chain-binding affinity substances. *See* Office Action at p. 13. Kawabata also teaches use of a buffer and a polymer, including negatively charged polymers, having a molecular sieve effect for separating complexes from unbound affinity substances. *See id.* As taught by Kawabata, the polymers used to fill the capillary are a separation media because they function to separate the sample components based on size differences. *See* Kawabata, paragraph [0057]. In fact, Kawabata limits the kind of polymers used in this connection to "polymers having a molecular sieving effect." *Id.* Thus, to the extent that Kawabata teaches the inclusion of a polyanion, it is only as the separation media, and not a polyanion specifically added to the separation media as required by claims 1, 39, 51, and 93. The polymer having a molecular sieve effect of Kawabata cannot serve as an anticipating disclosure of both the separation/concentration media *and* the separately added polyanion of the claimed invention. Kawabata therefore does not anticipate these claims because it does not disclose the elements of the claimed invention arranged as in the claim.

Further with regard to claim 39, the Office Action states that Kawabata teaches a first complex as required by claim 39, and further that the claim does not limit how the analyte is

labeled, so therefore the teaching by Kawabata would anticipate the claim. Office Action at p. 7. Applicants respectfully assert that the claim does limit how the analyte (or its analogue) is labeled. As set forth in step (i)(b), the claim includes the step of adding an already labeled analyte (or analogue) to the sample containing the (unknown amount) of analyte. This permits the labeled analyte to compete with the (unlabeled) analyte of interest in the sample for binding to the affinity molecules used in the claimed methods. This competitive binding format is illustrated in Figs. 3G-3K. *See also* paragraph [0148] of the specification. In contrast, the teaching by Kawabata does not suggest using prelabeled analytes (targets) that will compete with unlabeled analytes for binding sites. Moreover, Kawabata teaches that the label (marker) will ultimately form in situ once all the various components are mixed together. Finally, Applicants respectfully indicate that claim 39 embodies a competitive assay method, whereas Kawabata does not teach such a method, as discussed next with respect to claim 42.

Claim 42 also embodies a competitive assay method. *See* paragraph [0148], [0155], and [0082] of the specification. This method permits contacting either (a) the analyte, (b) the analyte bound to a charged carrier molecule, and (c) a detectably-labeled affinity molecule, or, in the alternative, (a) the analyte, (b) an analogue of the analyte bound to a charged carrier molecule, and (c) a detectably-labeled affinity molecule. As a result of contacting such a mixture, two types of complexes may form. The first complex is comprised of either the analyte bound to a charged carrier molecule and the labeled affinity molecule, or, in the alternative, an analogue of the analyte bound to a charged carrier molecule and the labeled affinity molecule. The second complex is comprised of the analyte in the sample and the labeled affinity molecule. It should be noted that the substances listed under item (b), the analyte or analyte analogue bound to a

charged carrier molecule, are conjugates prepared in advance of performing the method. *See, e.g.*, paragraphs [0155] and [0082]-[0104] of the specification.

In a competitive assay, an amount of a labeled analyte is added to the sample containing the analyte of interest. The labeled analyte (added to the sample) and the unlabeled analyte (present in the sample) then compete to bind with the labeled affinity molecule. Kawabata may teach the labeling and separation of two or more targets, but nowhere does Kawabata teach a competitive assay using targets that are prelabeled and added to the sample. Kawabata therefore does not anticipate this claim because it does not disclose the elements of the claimed invention arranged as in the claim.

Further with regard to claim 51, the Office Action states that Kawabata allegedly teaches a concentration channel. Office Action at p. 8. Even assuming, without acquiescing to the conclusion, that the channel leading from the sample reservoir towards the separation capillary is a concentration channel, Kawabata does not teach the use of a polyanion added to the concentration media, a limitation that is expressly recited in claim 51. Moreover, the Office Action does not indicate where Kawabata teaches the addition of a polyanion that serves the function recited in the claim. Without such a teaching, Kawabata fails to disclose at least one element of the claim, and therefore cannot anticipate the claim.

Further with regard to claim 93, the Office Action states that Kawabata teaches a method for measuring (detecting) a target separated by complexing with a nucleic acid chain-binding affinity substance. Office Action at p. 11-12. The Office Action does not, however, indicate where Kawabata discloses the addition of a polyanion to the separation media with the recited function of binding to interfering sample constituents. Without such a teaching, Kawabata fails to disclose at least one element of the claim, and therefore cannot anticipate the claim.

If an independent claim is not anticipated, none of its dependent claims can be anticipated either. *See* MPEP § 2131; *see also Hartness Int'l, Inc. v. Simplimatic Eng'r Co.*, 819 F.2d 1100, 1108 (Fed. Cir. 1987). Applicants respectfully maintain that independent claims 1, 39, 42, 51, and 93 are not anticipated by Kawabata for the reasons stated above. Therefore, claims 3-4, 9-14, 16-27, 29, 35, 37-38, 43-44, and 95-96, which depend from independent claim 1; claims 41, 98, and 99, which depend from independent claim 39; claim 100, which depends from independent claim 42; and claims 53, 55, 60-65, 67-75, 78, 86, and 92, which depend from independent claim 51, are also not anticipated by Kawabata.

Claims 15, 36, 40, 59, 83, 94, and 97 have been canceled by amendment. Accordingly, Applicants request that the rejection of these claims be withdrawn as moot.

For the above reasons, Applicants respectfully request that the rejection of claims 1, 3-4, 9-27, 29, 35-44, 51, 53, 55, 59-65, 67-75, 83, 86, 92-93, and 95-99 under § 102 be withdrawn.

II. Claim Rejections Under 35 U.S.C. § 103 - Obviousness

A. Claims 4, 8, 79, 84, and 91

Claims 4, 8, 79, 84, and 91 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Kawabata as applied to claims 1, 3-4, 9-27, 29, 35-44, 51, 53, 55, 59-65, 67-75, 83, 86, and 92-99, in view of Stalcup et al. ("Stalcup"). Applicants respectfully traverse these rejections for the reasons set forth below.

If an independent claim is nonobvious under 35 U.S.C. § 103(a), then any claim depending therefrom is nonobvious. *See* MPEP § 2143.03. As discussed above, Kawabata does not teach or suggest all the limitations of independent claims 1 and 51, from which claims 4, 8, 79, 84, and 91 depend. In particular, as discussed above, Kawabata does not teach the use of a polyanion added to the separation media that is separate and distinct from the separation media

itself or from the charged carrier molecule. Furthermore, the Office Action does not reject any independent claims as obvious over Kawabata in view of Stalcup. Because no independent claim stands rejected as nonobvious, dependent claims 4, 8, 79, 84, and 91 are also nonobvious.

The analysis for obviousness must consider whether the differences between the subject matter sought to be patented and the prior art are such that the subject matter *as a whole* would have been obvious at the time the invention was made to a person of ordinary skill in the art. *See* 35 U.S.C. § 103. To reject a claim under 35 U.S.C. § 103(a), all the claim limitations must be taught or otherwise suggested by the prior art, and there must be some articulated reasoning with some rational underpinning to support the conclusion of obviousness. *See* MPEP § 2142.

The Office Action states that Kawabata does not teach using heparin sulfate, for example, as the polyanion in the method, and that Stalcup only supplements the disclosure of Kawabata with the teaching that an electrophoresis running buffer can contain 2% heparin. Office Action at p. 14. Applicants respectfully disagree that the disclosure in Stalcup of using 2% heparin in a phosphate running buffer used for capillary zone electrophoresis renders claims 4, 8, 79, 84, and 91 obvious. The Office Action admits that Stalcup does not teach adding heparin to the separation media. Office Action at p. 16. Instead, the basis given for the rejection is that one of skill in the art would substitute heparin as the polyanion in Kawabata's disclosure of a separation media and a polyanion to arrive at the subject claims. *Id.* However, the polyanions taught by Kawabata are "polymers having a molecular sieve effect," and these constitute the separation media. *See* Kawabata, paragraph [0057]. Stalcup does not teach or suggest using heparin for the purposes taught by Kawabata. Stalcup only teaches that heparin's anionic character enhances its solubility and may have considerable electrophoretic mobility, Office Action at p. 15, none of which suggests that it might used for a molecular sieve effect. Therefore, Stalcup's heparin

cannot substitute to serve the function required by Kawabata. The teaching by Stalcup about the benefits of using heparin also bears no relation to the use and function of the polyanion as recited in the subject claims.

The teachings of Stalcup and Kawabata do not suggest any reason to combine these references, and nor would their combination, considered as a whole, render the claims, considered as whole, obvious.

For the reasons stated above, Applicants respectfully request that the rejection of claims 4, 8, 79, 84, and 91 over Kawabata in view of Stalcup under § 103 be withdrawn.

B. Claims 31-32 and 88-89

Claims 31-32 and 88-89 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Kawabata as applied to claims 1, 3-4, 9-27, 29, 35-44, 51, 53, 55, 59-65, 67-75, 83, 86, and 92-99, in view of Stathakis et al. ("Stathakis"). Applicants respectfully traverse these rejections for the reasons set forth below.

If an independent claim is nonobvious under 35 U.S.C. § 103(a), then any claim depending therefrom is nonobvious. *See* MPEP 2143.03. As discussed above, Kawabata does not teach all the claim limitations of any independent claim. Furthermore, the Office Action does not reject any independent claims as obvious over Kawabata in view of Stathakis. Because no independent claim stands rejected as nonobvious, dependent claims 31-32 and 88-89 are also nonobvious.

The Office Action states that Kawabata does not teach a charged polymer with a concentration of about 0.01 to 5% or 0.001 to 1%, and that Stathakis only supplements the disclosure of Kawabata with the teaching that certain polymers can be used at such concentrations to coat a capillary wall. Office Action at p. 17. Applicants respectfully disagree

that the disclosure in Stathakis of using a coating of dextran sulfate or polyvinyl sulphonic acid on the walls of a capillary electrophoresis tube renders claims 31-32 and 88-89 obvious.

The basis given for the rejection is that one of skill in the art would modify the method of Kawabata to include the charged polymers of Stathakis because including such polymers can improve migration time. Office Action at p. 17-18. However, Stathakis explains that the study was carried out to test the effect of the hydrophobicity/hydrophilicity of a polymer on its ability to absorb onto the capillary wall. Stathakis, p. 230, Section 3.3. Thus, Stathakis teaches selecting polymers to counter wall effects in capillary electrophoresis based on its hydrophilicity. In contrast, Kawabata uses a polymer to fill the capillary, which thereby minimizes wall effects because the walls are already screened by the separation medium which fills the capillary. *See* Kawabata, paragraph [0057]. The method of Kawabata therefore teaches away from combining it with the teaching of Stathakis of using hydrophilic polymers to suppress the wall effects of a capillary column which lacks a separation medium.

Kawabata does not teach or suggest all the limitations of independent claims 1 and 51, from which claims 31-32 and 88-89 depend. In particular, as discussed above, Kawabata does not teach the use of a polyanion added to the separation media that is separate and distinct from the separation media itself or from the charged carrier molecule. Moreover, neither Kawabata nor Stathakis teach or suggest using a polyanion to bind interfering sample constituents to thereby reduce interference with the binding of such sample constituents to the charged carrier molecule as recited by the subject claims. Therefore these references, considered as a whole, do not render the claims, considered as a whole, obvious.

For the reasons stated above, Applicants respectfully request that the rejection of claims 31-32, and 88-89 over Kawabata in view of Stathakis under § 103 be withdrawn.

C. Claim 66

Claim 66 was rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Kawabata as applied to claims 1, 3-4, 9-27, 29, 35-44, 51, 53, 55, 59-65, 67-75, 83, 86, and 92-99, in view of Fukui et al. ("Fukui"). Applicants respectfully traverse these rejections for the reasons set forth below.

If an independent claim is nonobvious under 35 U.S.C. § 103(a), then any claim depending therefrom is nonobvious. *See* MPEP 2143.03. As discussed above, Kawabata does not teach all the claim limitations of any independent claim. Furthermore, the Office Action does not reject any independent claims as obvious over Kawabata in view of Fukui. Because no independent claim stands rejected as nonobvious, dependent claim 66 is also nonobvious.

Applicants respectfully disagree that the disclosure of Fukui of connecting ACMA to an oligonucleotide chain through tri-, tetra-, or pentamethylene linker renders claim 66 obvious. First, Kawabata does not teach or suggest all the limitations of independent claim 51, from which claim 66 depends for the reasons discussed above. The Office Action states that Kawabata does not teach a synthetic sequence consisting of a nucleotide that contains a methylene group in the place of the oxygen in the ribose ring. Office Action at p. 19. Furthermore, Fukui only supplements the disclosure of Kawabata with the teaching of the synthetic linker. *Id.*

Claim 66 recites in part using "a nucleotide that contains a methylene group in the place of the oxygen in the ribose ring." Replacing the oxygen of the ribose ring with a methylene group results in a cyclopentyl ring. In contrast, Fukui's linker is an acyclic methylene chain. No cyclic connector groups are disclosed by Fukui, other than ribose rings. Because Fukui does not disclose "a nucleotide that contains a methylene group in the place of the oxygen in the ribose

ring," all of the limitations of claim 66 are not found in the prior art, and therefore the claim cannot be obvious.

For the reasons stated above, Applicants respectfully request that the rejection of claim 66 over Kawabata in view of Fukui under § 103 be withdrawn.

D. Claims 57-58

Claims 57-58 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Kawabata as applied to claims 1, 3-4, 9-27, 29, 35-44, 51, 53, 55, 59-65, 67-75, 83, 86, and 92-99, in view of Kaniansky et al. ("Kaniansky"). Applicants respectfully traverse these rejections for the reasons set forth below.

If an independent claim is nonobvious under 35 U.S.C. § 103(a), then any claim depending therefrom is nonobvious. *See* MPEP 2143.03. As discussed above, Kawabata does not teach all the claim limitations of any independent claim. Furthermore, the Office Action does not reject any independent claims as obvious over Kawabata in view of Kaniansky. Because no independent claim stands rejected as nonobvious, dependent claims 57-58 are also nonobvious.

Applicants respectfully disagree that the disclosure in Kaniansky of using isotachophoresis as a concentration method prior to the separation step renders claims 57-58 obvious. First, Kawabata does not teach or suggest all the limitations of independent claim 51, from which claims 57-58 depend. In particular, as discussed above, Kawabata does not teach the use of a polyanion added to the separation media that is separate and distinct from the separation media itself or from the charged carrier molecule. The Office Action states that Kawabata does not teach using isotachophoresis, and that Kaniansky only supplements the disclosure of Kawabata with the teaching of the isotachophoresis method. Office Action at p. 21-22.

Regardless of whether it is proper to combine the teachings of Kawabata and Kaniansky, Kaniansky does not disclose at least one of the elements of the subject claims, the polyanion, shown to be absent from the disclosure of Kawabata. Accordingly, all of the limitations of claims 57-58 are not found in the prior art, and therefore the claims cannot be obvious.

For the reasons stated above, Applicants respectfully request that the rejection of claims 57-58 over Kawabata in view of Kaniansky under § 103 be withdrawn.

E. Claims 56-57

Claims 56-57 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Kawabata as applied to claims 1, 3-4, 9-27, 29, 35-44, 51, 53, 55, 59-65, 67-75, 83, 86, and 92-99, in view of Wolfe et al. ("Wolfe"). Applicants respectfully traverse these rejections for the reasons set forth below.

If an independent claim is nonobvious under 35 U.S.C. § 103(a), then any claim depending therefrom is nonobvious. *See* MPEP 2143.03. As discussed above, Kawabata does not teach all the claim limitations of any independent claim. Furthermore, the Office Action does not reject any independent claims as obvious over Kawabata in view of Wolfe. Because no independent claim stands rejected as nonobvious, dependent claims 56-57 are also nonobvious.

Applicants respectfully disagree that the disclosure in Wolfe of using adsorption as a concentration method prior to the separation step renders claims 56-57 obvious. First, Kawabata does not teach or suggest all the limitations of independent claim 51, from which claims 56-57 depend. In particular, as discussed above, Kawabata does not teach the use of a polyanion added to the separation media that is separate and distinct from the separation media itself or from the charged carrier molecule. The Office Action states that Kawabata does not teach using solid phase extraction (adsorption) methods, and that Wolfe only supplements the disclosure of

Kawabata with the teaching of the solid phase extraction method. Office Action at p. 23-24. Regardless of whether it is proper to combine the teachings of Kawabata and Wolfe, Wolfe does not disclose at least one of the elements of the subject claims, the polyanion, shown to be absent from the disclosure of Kawabata. Accordingly, all of the limitations of claims 56-57 are not found in the prior art, and therefore the claims cannot be obvious.

For the reasons stated above, Applicants respectfully request that the rejection of claims 56-57 over Kawabata in view of Wolfe under § 103 be withdrawn.

III. Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully request entry by the Examiner of this Amendment under 37 C.F.R. § 1.111, reconsideration of this application, and the timely allowance of claims 1, 3-4, 8-14, 16-27, 29, 31-32, 35, 37-39, 41-44, 51, 53, 55-58, 60-75, 78-79, 84, 86, 88-89, 91-93, 95-96, and 98-100. Applicants submit that the proposed amendments to the claims do not raise new issues or necessitate the undertaking of any additional search of the art by the Examiner, since all of the elements and their relationships were either claimed earlier or inherent in the claims as examined. Therefore, this Amendment should allow for immediate action by the Examiner.

Respectfully submitted,

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Dated: December 19, 2008

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